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NALOXONE - DOES OVER-ANTAGONISM MATTER? EVIDENCE OF IATROGENIC HARM AFTER EMERGENCY TREATMENT OF HEROIN/OPIOID OVERDOSE

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The original study was funded by the Scottish Office. Joanne Neale is now part-funded by, and John Strang is supported by, the National Institute for Health Research (NIHR) Biomedical Research Centre for Mental Health at South London and Maudsley NHS Foundation Trust and King's College London. John Strang is a clinician and has had, and continues to have, clinical responsibilities and has also worked with a range of types of treatment and rehabilitation service-providers. He has also worked with pharmaceutical companies to seek to identify new or improved treatments, and also with a range of governmental and non-governmental organisations to advocate for consideration of wider naloxone provision. A fuller account is given on his personal university webpage at: <http://www.kcl.ac.uk/ioppn/depts/addictions/people/hod.aspx> The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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ABSTRACT

Aim To analyze drug users' views and experiences of naloxone during emergency resuscitation after illicit opiate overdose in order to identify i. any evidence of harm caused by excessive naloxone dosing ('over-antagonism'); ii. implications for the medical administration of naloxone within contemporary emergency settings.

Design Re-analysis of a large qualitative dataset (interviews and non-participant observation) generated between 1997 and 1999.

Setting Emergency departments, drug services and pharmacies in two Scottish cities.

Participants 200 illicit opiate users: 131 males; 69 females.

Findings Participants had limited knowledge of naloxone and its pharmacology, yet routinely described it in negative terms and were critical of its medical administration. In particular, they complained that naloxone induced acute withdrawal symptoms, causing patients to refuse treatment, become aggressive, discharge themselves from hospital, and take additional street drugs to counter the naloxone effects. Participants believed that hospital staff should administer naloxone selectively and cautiously and prescribe counter-naloxone medication if dosing precipitated withdrawals. In contrast, observational data indicated that participants did not always know that they had received naloxone and hospital doctors did not necessarily administer it incautiously.

Conclusions Opiate users repeatedly reported harm caused by naloxone over-antagonism. Good treatment in emergency settings involves building and sustaining trust with patients and those who accompany them. Protocols are needed for titrating naloxone dose against response to prevent sudden acute withdrawal syndrome, with attendant risks of self-discharge, further drug use and even death. The concept of contemporary legend helps to explain why naloxone had such a poor reputation amongst opiate users.

Key words: qualitative study, naloxone, overdose, opiates, contemporary legend

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INTRODUCTION

Naloxone saves lives when given by emergency medical staff in accident and emergency departments and by ambulance personnel attending overdoses in the community.¹⁻³ Over the last decade, naloxone distribution programmes have been introduced, as public health initiatives and individual health treatments, to prevent heroin/opioid overdose deaths,⁴⁻¹⁷ Programmes involve the supply of naloxone (plus training in wider overdose management) to drug users and to their families, enabling interim emergency care while awaiting the arrival of an ambulance.^{18 19}

NHS England recently issued a Patient Safety Alert (NHS/PSA/W/2014/016; 20 November 2014) on '*Risk of distress and death from inappropriate doses of naloxone in patients on long-term opioid or opiate treatment*'. This alert primarily addressed risk in relation to the treatment of pain in older people, but warned that: "*Use of naloxone in patients where it is not indicated, or in larger than recommended doses, can cause a rapid reversal of the physiological effects for pain control, leading to intense pain and distress, and an increase in sympathetic nervous stimulation and cytokine release precipitating an acute withdrawal syndrome.*" Amongst dependent opiate users who have overdosed, naloxone can also cause sudden-onset acute withdrawal syndrome with evidence of aggression²⁰ and medical self-discharge.^{21 22}

Since patient safety is uncertain when hospital admission does not occur after naloxone administration for acute opioid toxicity²³, clinical algorithms to support discharge decision-making have been developed.²⁴⁻²⁷ Dose and route are not, however, agreed, with quantities given ranging from 0.4mg^{3 27} to 2mg or more.¹ Several studies have found no evidence of deaths after self-discharge^{24 27-30}, but weaknesses in these studies have been identified.²⁷ Furthermore, a recent European analysis reported a small incidence of post-naloxone mortality (3/2241; 0.13%) which was attributed to 'rebound opioid toxicity'.²² The clinician

is thus 'walking a prescribing tightrope'³ between adequate resuscitation and precipitation of acute withdrawals with attendant risks of self-discharge and subsequent harm.

Better understanding of opiate users' views and experience of emergency naloxone is needed to support medical care and decision-making, and to inform the wider pre-supply of naloxone, as recently advocated by World Health Organization, United Nations and others.¹⁶

³¹ ³² In the absence of any current or recent research exploring this issue, we have returned to an earlier ethnographic study of non-fatal overdose to seek insights. In so doing, our aim is to analyze opiate users' views and experiences of naloxone during emergency resuscitation in order to identify i. any evidence of harm caused by excessive naloxone dosing ('over-antagonism') and ii. implications for the medical administration of naloxone within contemporary emergency settings.

METHOD

The study was undertaken between 1997 and 1999 and the lead researcher (JN) is a current author. Findings relating to naloxone were discussed briefly in a publication written at the time and included cautionary warnings that opiate users tended to hold very negative views of the antagonist, believed that it could induce painful withdrawal symptoms, and were anxious that it might be administered to them.³³ Despite this, no detailed analyses of naloxone were undertaken.

Fieldwork occurred in two Scottish cities known for their high levels of illicit drug overdose. Qualitative interviews were conducted with 200 opiate users, over a third of whom were interviewed and observed in the emergency department or acute hospital ward within a few hours of an overdose occurring. Individuals were recruited in two groups. *Group A* participants (n=77) were purposively sampled through six hospital emergency departments. *Group B* participants (n=123) were opportunistically sampled through drug agencies, pharmacies providing services to drug users and snowballing.

All 200 participants were current users of heroin, methadone and/ or dihydrocodeine, but other types of drug taking were common. In total, 153/200 (77%) had ever personally

overdosed: 76 (99%) group A participants and 77 (63%) group B participants. Further demographic information is provided in Table 1. Ethical approval was granted from six NHS research ethics committees; details previously reported.³⁴

INSERT TABLE 1

Group A interviews were conducted at all hours of the day and night, most frequently between 9pm and 1am. Hospital staff telephoned the researcher whenever an individual arrived in the emergency department with symptoms of illicit drug overdose. The researcher was available 24/7 for thirteen months. Seventy interviews were conducted in the 6 hospitals and 7 took place later, in the drug user's home or local drug service. Group B interviews all occurred during the day or early evening and were conducted in drug agencies, cafes, public houses, shopping malls and the researcher's car.

Interviews lasted 20-90 minutes, were audio recorded and transcribed verbatim. The interview schedule covered: *biographical details; current and past drug use; participation in treatment; overdoses experienced; overdoses witnessed; general opinions about overdose; and additional comments*. The same core topics were introduced in each interview, but participants were encouraged to reflect on and discuss issues that were most relevant to them personally. Although 47 participants had never personally overdosed, nearly all had witnessed an overdose and everyone had views on overdosing.

Transcribed interview data and fieldnotes were indexed at the time of the study using the software package WinmaxPro (now MAXQDA) and analysed using 'Framework'.³⁵ For the present analyses, all data previously indexed to a broad generic code 'naloxone' were exported to a single Microsoft Word document for re-analysis, again using the principles of Framework. First, JN reviewed the naloxone Word file line-by-line, systematically ordering the findings under emergent headings. Both authors then reviewed, discussed and revised the ordered data, creating six inter-linked core themes (see Findings below). JN next returned to the coded data to check the core themes for internal validity, to map the range and nature of data under each core theme, and to explore any differences between sub-groups of participants. Lastly, both authors interpreted the findings with reference to naloxone administration, identifying the concept of contemporary legend as a useful explanatory

heuristic.

In our reporting, we have used non-specific forms of semi-quantification ('many', 'several', 'a few') to convey general patterns within the data, reserving raw numbers and more precise quantitative terms only for those occasions when findings could be reliably quantified.³⁶ Differences between sub-groups of participants are recorded where identified. As with any qualitative research, empirical findings cannot be generalizable beyond the study population.

FINDINGS

(i) General knowledge of naloxone

Approximately a third of all participants (from groups A and B) had not heard of naloxone (or its street names) and did not recognize it from the researcher's description of when, how and why it was used. Several participants (again from both groups) said that they were aware of the drug but then appeared to confuse it with amphetamine sulphate ('speed'). Others, who had seen intracardiac injection scenes in popular films such as 'Pulp Fiction', wrongly believed that naloxone was adrenaline, administered violently via 'a large needle' into the hearts of overdose victims.

Fieldnote: Barry asks the doctor about the needle that was put into his heart last time he was in the emergency department. The doctor says that this was unlikely and Barry must be confused. [Barry, 29 years, group A]

Few participants knew naloxone by its generic or trade name, Narcan. However, nearly all recognized it when the researcher used street terms, such as 'the jag', 'adrenaline', or 'the reverse', or when she provided more detail on its use. Whilst injectors and participants who had friends or relatives who were also opiate users seemed more likely to have heard of naloxone than other study participants, there was no discernible pattern of knowledge relating to whether or not someone had personally had an overdose or ever injected.

Participants who had heard of naloxone mostly had very limited knowledge of its pharmacology; essentially, they knew that it rapidly reversed the effects of a heroin overdose in an emergency situation. Several individuals volunteered further details. For example, a few reported that the antidote 'dulled' the effects of any illicit drugs subsequently taken, so increasing an individual's propensity to overdose if they used street drugs post administration. Three commented that the amount of naloxone administered to an overdose victim should depend on the quantity of heroin and other drugs taken and one also emphasized that the consequences of getting this wrong could be very dangerous.

I can't imagine what it would be like if they [hospital staff] injected Narcan on a small dose of heroin and put you into withdrawal. The psychological effects of that must be terrible... I could see people committing suicide. [Adam, 28 years, group A]

(ii) Personal experiences of naloxone

It was not possible to ascertain the actual number of participants who had ever received naloxone, since many did not know what naloxone was. Nonetheless, 74 (47 men; 27 women) believed they had been treated with naloxone at some point in their lives (some on many occasions). Individuals who stated that they had personally had naloxone frequently complained that it had made them feel 'horrible' or very unwell, and had induced acute opiate withdrawal symptoms, such as shaking, headaches, and vomiting, sometimes lasting several days.

They gave me that injection, that, er, reverse, and I woke up absolutely shaking... It was like instant withdrawals. It was the most horrendous experience that I've ever been through. [Beverley, 33 years, group A]

Hellish... I was in my bed for about three days after it. [I] couldn't move, being sick... I was really ill. Cramps, everything. [Francis, 22 years, group B]

These naloxone-induced withdrawal symptoms were sometimes so severe that participants reported going 'mad' or 'crazy' or losing their temper and becoming aggressive or violent

with hospital staff, particularly if they had explicitly requested not to be treated with the antidote.

I said to them [hospital staff], 'Please don't give me adrenaline'. And he [doctor] said 'No, I'm not going to give you adrenaline'. [And he] stuck the needle in my arm. And I knew because I felt the tingling in my foot. And that's when I went crazy... Grabbed the metal side of the bed and I was kicking it and screaming and pulling my hair out. [Rab, 25 years, group B]

(iii) Personal responses when offered naloxone

Prior negative experiences of naloxone seemed especially relevant when considering group A participants' reactions to naloxone at the point of their current overdose. Few willingly accepted naloxone if they were conscious. Most refused the drug or reported that they would have refused it if they had been offered it. Indeed, many did their utmost to avoid naloxone by, for example, discharging themselves from hospital whilst waiting for a doctor to arrive or trying to force themselves to stay conscious and alert when nurses were around.

Fieldnote: At about 11pm the doctor arrived and suggested Narcan. Mary reacted very negatively and threatened to leave... Mary washed her face in the sink and tried to revive herself. The nurse returned and Mary refused the Narcan but agreed to wait for the blood test results. [Mary, 22 years, group A]

In practice, group A participants had sometimes been given naloxone whilst unconscious or too ill to be able to refuse treatment. Moreover, some had been given multiple doses over several hours. These individuals often reported that they had not been given naloxone, even though friends or relatives present, hospital staff, hospital notes, or the researcher's own observations indicated otherwise. In none of these situations, did the researcher record any evidence of withdrawal symptoms and the participants themselves did not report any. On the contrary, several stated that they were starting to feel better since arriving at the hospital and receiving treatment.

Fieldnote: Majorie cannot remember having a naloxone injection, although the hospital staff said that she had...

Participant: They were going to give me Narcan, but I didn't want it. I started screaming.

Researcher: So you didn't get any?

Participant: No... I would have marks on me if I had, because they'd have had to get a vein... If I'd had narcan, I'd have been shivering now. I've not had it. [Marjorie, 28 years, group A]

(iv) Further drug use to counter the effects of the naloxone

Thinking back to their previous overdoses, four participants (2 from group A; 2 from group B) described how, after being treated with naloxone, they had discharged themselves from hospital because they felt that they needed to take more street drugs to offset the withdrawals. As they neither had drugs nor money with them in the hospital, this meant that they had first had to obtain money and then find a dealer.

I just bolted. Signed myself out [of hospital]. I came home... got a loan of a tenner [£10] off somebody... and I just went out and got another one [deal of heroin]. [Willy, 29 years, group B]

One participant (group A) had also consumed a considerable amount of alcohol and then gone to a local drug treatment service for help. Another reported that he had broken into a drug dealer's house and robbed him. Two group B participants also reported that their withdrawal symptoms had been so severe that hospital staff had prescribed them methadone or lofexidine to counter the naloxone they had been given. One of these had then supplemented this with methadone he had stored at home. Several participants also stated that concern about having to take more drugs to counter any naloxone received was a major factor in their refusal of the treatment.

Researcher: If someone offered you that [naloxone] again, would you take it?

Participant: No definitely not.

Researcher: Why not?

Participant: Because it's instant withdrawals and then when I go out of here [hospital], the first thing I would do is look for something else to take that pain away.

[Beverley, 33 years, group A]

(v) General views of naloxone

Almost all participants who had heard of naloxone described it in very negative terms, emphasizing how it should be avoided since it caused instant and unpleasant withdrawal symptoms: it 'takes your stone away', 'strings you out', 'makes you rattle', 'is instant hangout', 'makes you feel sick', 'causes a headache', 'ruins the hit', and 'makes you feel worse'. Indeed, so pervasive was the belief that naloxone inevitably caused withdrawal symptoms that one person whose friend had been treated for an overdose and yet not experienced withdrawal symptoms believed that the friend must have been given a different treatment, not naloxone.

They've got a new one [drug] out now that makes you feel alright. You don't feel strung out when you take it... Somebody I was in hospital with got it, and he thought he was going to be strung out..., and he says he was fine after it. [Benjamin, 25 years, group B]

Supporting their own views, participants often described the adverse reactions of their friends, relatives, and acquaintances (sometimes witnessed first-hand and sometimes based on second-hand or third-hand accounts). Thus they spoke of other drug users also refusing to go to hospital, 'climbing out of the back of ambulances', 'signing themselves out of hospitals', and being in withdrawal for several days post naloxone administration. One participant even described how a friend had left hospital, taken more drugs, and then died.

Elaborating further on their dislike of naloxone, participants sometimes argued that drug users want to be 'stoned not sober' and 'prefer to sleep opiates off rather than be resuscitated'. Consequently, those who overdosed might not be grateful for any medical intervention. On the contrary, they might be angry as treatment with naloxone would mean

that they had effectively 'wasted their money' and would now need to go out and commit more crime in order to get drugs.

Anybody waking up and being totally right into withdrawals would be angry. And the possibility is they've spent all their money and they've not got money to get anything else. [Suzanne, 31 years, group B]

Despite these very negative views, some participants still thought that naloxone should be administered to overdose patients contrary to their wishes as it was necessary to save their lives. Equally, several argued that naloxone was a 'good thing' or a 'good idea'. These included a small number of individuals who had never heard of naloxone until the researcher described it to them in the interview and also a few participants (from both groups A and B) who had previously been treated with the antidote and had subsequently felt better.

I think it's a good idea. Because anybody that's overdosed, they're still alive... I felt brand new after it [naloxone injection]. I just felt normal. [Drew, 32 years, group B]

(vi) Opinions on medical practice

In total, seven participants (from groups A and B) gave angry accounts of opiate users (themselves or others) regaining consciousness and finding paramedics or hospital staff standing over them about to inject naloxone. Medics had then attempted to proceed with the injection contrary to the patient's wishes, resulting in disagreements and physical struggles.

Because they gave me something in the ambulance, but they were holding me down because I didn't want them to put it in my arm. [Patrick, 27 years, group A]

Two group A participants were annoyed that hospital staff had told them that they had not had the antidote, when they strongly believed that they had had it. Additionally, another group A participant criticized hospital staff for trying to give her naloxone without telling her enough about the drug and its side effects. One group B male further complained that he had been given naloxone as a punishment and to deter him from using heroin in the future.

Participants' accounts indicated that these negative experiences undermined patient trust in medical practice, so increasing the potential for hostility and violence.

When I got that adrenalin... I was up to the hospital two days in a row with a tin of CS gas and a butterfly knife... I was going to stab the doctor for doing that to me. I was coming out of it [the overdose], waking up... I know the only reason they did it was to put me off heroin. [Dougie, 27 years, group B]

Consistent with their generally negative views of naloxone, several participants stated that the drug should be given more cautiously and selectively; not against a patient's wishes and certainly not if the patient was already conscious. Others argued that hospital staff should dispense methadone or other medication to counter naloxone-induced withdrawals, thus lessening the likelihood that patients would be anxious and refuse to be admitted to hospital. Interestingly, no participant reported that medics might ever consider but then decide not to administer naloxone. Yet, the researcher recorded several instances of doctors being unsure that the patient had actually taken opiates and so concluding that naloxone was inappropriate or deciding that it would be better for the patient to sleep their drugs off on the ward.

Notwithstanding a general hostility to medical practitioners, a small number of participants from both groups A and B maintained that paramedics and hospital staff were only trying to help overdose patients by administering naloxone and so it was unfair to be angry with them. In addition, one participant recounted a recent positive experience of being at the hospital with a friend who had overdosed. The friend had not wanted naloxone because he did not want to experience withdrawal symptoms overnight in hospital. However, a nurse had taken time to explain that that would not happen. The friend had then accepted the naloxone and recovered well.

DISCUSSION

Opiate users repeatedly reported harm caused by naloxone over-antagonism. Naloxone was perceived very negatively by the study participants who emphasized its adverse effects, including acute withdrawal symptoms with associated aggression towards hospital staff,

refusal of treatment, premature self-discharge from medical care, and the need to obtain and take further illicit drugs. These critical views derived from their first-hand experiences and second-hand and third-hand accounts. Paralleling their reports of naloxone's harmful effects, participants additionally provided descriptions (self-report and anecdotal) of poor treatment by medical staff, including suggestions that naloxone was administered unnecessarily, in excess of that required, and even as a deterrent to (and possible punishment for) continued drug use.

Negative views of naloxone and accounts of harm caused by its administration were not, however, universal and were notably absent from the observational data. This discordance can be examined in conjunction with participants' lack of knowledge and confusion about naloxone; for example, Barry's seemingly mistaken belief that he had had the emergency drug injected directly into his heart and participants' certitude that they had not received naloxone when administration had been observed by the researcher or reported by others present. This is not to suggest that participants deliberately falsified their accounts. We are simply reminded that personal belief and testimony may not always coincide with reality ('veridicality').³⁷ 'Antagonistic' administrations of naloxone clearly occurred; yet, naloxone also saved lives and its administration did not inevitably cause harm or generate patient distress.

Before turning to the practical implications of our analyses, it is important to try to understand why naloxone had such a poor reputation amongst these Scottish opiate users. The concept of contemporary legend is not perfect, but offers a useful heuristic for explaining the findings. Contemporary legends constitute a form of folklore that can be based on fact, tend to be spread by word of mouth, and are often believed to be true by the tellers.³⁸⁻⁴² They are flexible narratives that provide individuals with a means of communicating and negotiating genuine fears and unexplained experiences.^{39 43} For our interviewees, accounts of antagonistic naloxone administration appeared to facilitate the expression of legitimate anxieties about overdosing, poor medical treatment, stigmatizing attitudes, painful withdrawal symptoms, and the difficulties of drug procurement. In a context where knowledge of naloxone was poor and mistrust between drug users and hospital staff already existed³³, few 'antagonistic' administrations would be necessary to create a 'received wisdom' of hostile intent that fuelled negative expectations.

Our analyses were based on 70 face-to-face interviews conducted within a few hours of heroin/opioid overdose occurring, supplemented by observations from hospital settings and a further 130 interviews. Although participants were recruited from only two cities in Scotland, their gender and age profile was broadly similar to that identified in other national and international studies of drug overdose at the time.⁴⁴⁻⁴⁶ Sampling was purposive (group A) and opportunistic (group B), rather than sequential or randomized. Nonetheless, the study captured a substantial number of overdose resuscitations in the two localities over the study period. No individual approached within any emergency department refused to participate, and so no selection bias occurred on the part of the overdose victims themselves. In support of our findings, opiate users' misconceptions about naloxone and negative views of its impact and use have also since been reported in another smaller qualitative study conducted in the US.⁴⁷

Ultimately, however, our data were collected in 1998/9 and the relevance of our findings to contemporary emergency care needs to be considered carefully. Today, the acceptability and uptake of naloxone have increased significantly, as evidenced by the widespread introduction of naloxone programmes, including peer driven and community-based programmes.⁴⁸ Indeed, there is a certain irony that the data we present are from Scotland, where the world's first national naloxone programme was later launched. Despite this, we cannot assume that positive perceptions and more sensitive administrations of the antagonist exist everywhere and amongst all stakeholders, particularly given that naloxone programmes are only now emerging in most of the world.^{16 32} Accordingly, we believe that themes evident in our data, and the explanatory concept of contemporary legend, still have important implications for contemporary emergency practice.

Crucially, our findings attest to the power of belief and folklore over lived experience, reminding us that instances of negative medical events (however rare or unlikely) can have a disproportionately harmful impact when they do occur. In addition to painful withdrawal symptoms, over-antagonism can result in reputational damage to the emergency services and their resuscitation efforts, such that individuals may discharge themselves prematurely or even refuse to consent to treatment. Thus, naloxone is transformed from a life-saving medication delivered by caring practitioners into a painful and withdrawal-precipitating

punishment administered by a hostile workforce. This is exacerbated by poor knowledge and understanding of naloxone amongst opiate users, insensitive and coercive medical administrations, lack of communication about the antagonist at the point of treatment, and pre-existing mistrust between drug users and medical staff.

In response, we suggest that it is incumbent on those working in emergency settings to look beyond the immediate resuscitative value of naloxone. Good treatment involves building and sustaining trust with patients and those who accompany them, providing clear information on how the antagonist works and its potential side effects, and being sensitive to patients' likely and understandable fears and concerns. In addition, more attention needs to be paid to protocols for titrating naloxone dose against response in order to prevent sudden acute withdrawal syndrome, with the attendant risks of self-discharge, further drug use and even death. As previous commentators have observed^{9 27}, the research literature is disappointingly weak on the dose-response relationship and the influence of individual variability. Until this knowledge gap is addressed, clinicians should seek to reverse life-threatening respiratory depression without clearing the opiate receptors so comprehensively that full-blown opiate withdrawal syndrome is precipitated.

The timely emergency administration of naloxone to an unconscious heroin/opiate overdose victim can unquestionably be good medical practice. However, providing this life-saving intervention in a way that triggers post-resuscitation distress and suffering can diminish its benefit, damage its reputation, and undermine patient/doctor trust. Medical decisions made about individual opiate overdose patients today can influence the future behavior of those same individuals, but also the behaviour of others within their wider networks. In this regard, it does not matter whether circulating accounts of naloxone are right, wrong, or an exaggeration of the truth. The concept of contemporary legend facilitates understanding of the genesis of community beliefs and how they can influence help-seeking, consent to treatment, interactions between drug users and medical staff, risk of rebound toxicity¹⁹ and compound overdose. Importantly, though, the telling and re-telling of horror stories about naloxone and its administration are not inevitable. Contemporary legends are dynamic and open to revision. Competent care and user participation in new naloxone training programmes, such as those recently introduced in Scotland^{17 49 50}, provide valuable opportunities for, and have already demonstrated some success in, changing harmful legends.

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TABLE 1: PARTICIPANT DETAILS

Demographic characteristics	Group A n = 77	Group B N = 123	All n = 200
Gender			
<i>Male</i>	54 (70%)	77 (63%)	131 (66%)
<i>Female</i>	23 (30%)	46 (37%)	69 (35%)
Mean age (years)	27 (range 15-47)	28 (range 17-45)	28 (range 15-47)
Mean age of first use (years)	16 (range 5-32)	16 (range 7-32)	16 (range 5-32)
Mean years of use	11 (range 1-27)	12 (range 1-31)	12 (range 1-31)
Ever overdosed			
<i>Yes</i>	76 (99%)	77 (63%)	153 (77%)
<i>No</i>	1 (1%)*	46 (37%)	47 (24%)
Ever injected**			
<i>Yes</i>	58 (75%)	94 (76%)	152 (76%)
<i>No</i>	18 (23%)	29 (24%)	48 (24%)
Ever used heroin			
<i>Yes</i>	61 (79%)	99 (81%)	160 (80%)
<i>No</i>	16 (21%)	24 (20%)	40 (20%)

* One male was interviewed in the emergency department after cutting his wrists. He had witnessed overdoses but never personally had an overdose

** Missing = 1